REMARKS

Status of the claims

Claims 57, 63, 64, 66, 68-71 and 87-102 were pending as shown in the paper filed March 14, 2007. The amendments to claim 57 and 91 made in the Response After Final filed August 27, 2007, were not entered because they were alleged to add new matter. In addition, the Advisory Action alleged that support for the amendments indicating that the cellular chromatin is within a cell was not found in the original recitation "cellular" chromatin; at page 10, lines 7-9 and original claim 53. See, page 2 of Advisory Action. Applicants note herein that support of this recitation is found in original 54 and on page 1, lines 11 and 15; and Examples 6, 9, 11, 12, 14 and 15, which describe introduction of non-naturally occurring exogenous molecules into a cell and demonstrate that these molecules bind to cellular chromatin within the cell.

Thus, claims 57, 63, 64, 66, 68-71 and 87-102 are pending and claims 57, 63, 64, 66, 68-71 and 87-90 are under consideration. Inasmuch as withdrawn claims 91-102 have been amended to contain all of the limitations of the elected composition claims, they are eligible for rejoinder upon allowance of the claims under consideration.

35 U.S.C. § 101

Claims 57, 63, 64, 66, 68-71 and 87-90 were again rejected under 35 U.S.C. § 101 as allegedly directed to non-statutory subject matter (Final Office Action, paragraph 2). In particular, it was alleged that these claims are product-by-process claims and "do not sufficiently distinguish over chromatin complexes with proteins as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products." *Id.*

Claim 57 (from which all other claims directly or ultimately depend) has been amended herein to make explicit that the exogenous molecule is a non-naturally occurring molecule and that cellular chromatin is within a cell (claim 57, emphasis added):

> A complex between a **non-naturally occurring exogenous** molecule and a binding site in cellular chromatin **within a cell**, wherein the binding site comprises a target site and is in a region

of cellular chromatin that is sensitive to a probe of chromatin structure.

Thus, the claimed complexes are clearly set forth in the hand of man in the fact that the exogenous molecule of the complex is non-naturally occurring. Accordingly, the rejection may be withdrawn.

35 U.S.C. §§ 102

A. Boyes

Claims 57, 63, 64 and 87-90 were again rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Boyes in light of Morceau and Hays and Gregory. (Final Office Action, paragraph 4). The Final Office Action states that Boyes shows that the binding of GATA-1 fragments to reconstituted chromatin results in disruption of the chromatin structure. *Id.* The Office then cites Morceau as allegedly demonstrating that GATA-1 is a zinc finger protein; Hays as showing that chromatin structure can be probed by chemical probes; and Gregory for showing that chromatin structure can be probed by restriction endonucleases. *Id.*

The pending claims relate to complexes between a non-naturally occurring exogenous molecule and a binding site in cellular chromatin within a cell. By contrast, and as acknowledged in the Final Office Action, all of the experiments described by Boyes are conducted *in vitro*, on reconstituted nucleosomes, not on cellular chromatin within a cell as claimed. See, for example, Boyes, page 530, first sentence of right column. Thus, Boyes does not anticipate the claimed subject matter.

B. Stamatoyannopoulos

Claims 57, 63, 64, 66, 68, 70, 71 and 87-90 were again rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Stamatoyannopoulos in light of Morceau and Hays and Gregory. (Final Office Action, paragraph 5). Stamatoyannopoulos was cited as previously for teaching analysis of a GATA-1 binding site in the human beta globin locus control region (LCR) as well as analysis of two types of cells: one (MEL) which is stably transformed with constructs of the LCR in which the GATA-1 binding site in the LCR is

either mutated or normal, and is analyzed by use of DNase I; and another (Namalwa) comprising a human LCR region analyzed using micrococcal nuclease. *Id.* Morceau, Hays and Gregory were cited as above with regard to Boyes.

To reiterate, the claims are drawn to complexes comprising a non-naturally occurring exogenous molecule bound to cellular chromatin within a cell. By contrast, Stamatoyannopoulos discloses GATA-1, a naturally occurring endogenous molecule. *See*, for example, Stamatoyannopoulos at page 108, first column: "An important property of these [MEL] cells is that they preferentially express GATA-1 . . ." and Stamatoyannopoulos at page 113, first column, first (incomplete) paragraph: "Because MEL cells almost exclusively express GATA-1 [*citation omitted*], our results imply that this particular GATA binding factor is functional in HS formation." Thus, this reference fails to describe or demonstrate a complex as claimed comprising a non-naturally occurring exogenous molecule, as claimed. Accordingly, the rejection should be withdrawn.

C. Truss

Claims 57, 63, 66, 70, and 87-90 were newly rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Truss in light of Beato. (Final Office Action, paragraph 6). Truss, in light of Beato, was cited for showing a complex between a steroid hormone receptor and chromatin. *Id.*

Truss discloses only naturally-occurring endogenous molecules (i.e., steroid hormone receptors and receptor-steroid complexes). This is unlike the claimed complexes which recite non-naturally occurring exogenous molecules. Accordingly, Truss does not anticipate the pending claims and the rejection may be withdrawn.

35 U.S.C. §§ 103

Claims 57, 87 and 90 were also again rejected under 35 U.S.C. § 103(a) as allegedly obvious over Boyes in view of Hays in view of Gregory. (Final Office Action, paragraph 9). Boyes, Hays and Gregory were cited as above with regard to 35 U.S.C. § 102 and it was alleged that it would have been obvious to the skilled artisan to determine

the chromatin structure of the complex of Boyes using the probes of Hays or Gregory and that, if such were done, it would establish that the complexes disclosed by Boyes are a species of the subject matter recited in claims 57, 87 and 90. *Id.*

Claims 57, 87 and 90 were also rejected under 35 U.S.C. § 103(a) as allegedly obvious over Stamatoyannopoulos in view of Hays and Gregory. (Final Office Action, paragraph 10). Stamatoyannopoulos, Hays and Gregory were cited as above regarding the 102(b) rejection. *Id.* It was alleged that it would have been obvious to determine the chromatin structure of the complex of Stamatoyannopoulos by use of the probes of Hays and/or Gregory and that, if such were done, it would establish that the GATA-1 complexes disclosed by Stamatoyannopoulos are a species of the subject matter recited in claims 57, 87 and 90. *Id.*

Claims 57, 66 and 69 were also rejected under 35 U.S.C. § 103(a) as allegedly obvious over Stamatoyannopoulos in view of Greisman. (Final Office Action, paragraph 11). It was again maintained that it would have been obvious to modify the complex of Stamatoyannopoulos by use of a complex of a zinc finger protein with chromatin in a plant cell in view of Greisman. *Id.*

Applicants respectfully submit the claims are indeed patentable over the cited combination and traverse the rejection and the Office's supporting remarks.

The Supreme Court in *KSR Int'l Co. v. Teleflex, Inc.*, No 04-1350 (U.S. Apr. 30, 2007) reaffirmed the viability of the four factual inquiries underlying an obviousness analysis provided in *Graham v. John Deere*, 148 USPQ 459, 467 (U.S. 1966). These factors include: (a) determining the scope and contents of the prior art; (b) ascertaining the differences between the prior art and the claims in issue; (c) resolving the level of ordinary skill in the pertinent art; and (d) evaluating evidence of secondary considerations. Moreover, the Supreme Court in *KSR* recognized that the "teaching, suggestion, or motivation" analysis provides a helpful insight in determining whether the claimed subject matter is obvious. This analysis is provided in MPEP 2142. In particular, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Additionally, there must be a

reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. Both the teaching or suggestion to make the claimed combination, as well as the reasonable expectation of success, must be found in the prior art, not in applicant's disclosure. See, e.g., *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991). Based on the foregoing, applicants respectfully submit the Office has failed to establish a *prima facie* case of obviousness.

The present claims are directed to complexes of non-naturally occurring exogenous molecules and cellular chromatin within a cell. The cited art does not teach or suggest this combination. Boyes teaches away from any complexes formed within a cell, clearly performing experiments on reconstituted chromatin. In addition, both Boyes and Stamatoyannopoulos relate to naturally occurring endogenous proteins that bind to chromatin and, accordingly, teach away from complexes comprising non-naturally occurring exogenous molecules as claimed.

The Examiner cites Hays and Gregory for teaching "probes" for chromatin. However, the probes of these references do not form complexes with chromatin as claimed and nothing can be gleaned from these references regarding a complex as claimed by applicants. Moreover, because the primary references teach away from complexes as claimed, the combination of references does not support the rejection.

In sum, the combination cited by the Office does not provide evidence that the claimed complexes are a "predictable use of prior art elements according to their established functions." *KSR*, page 13. Rather, as explained above, the evidence is to the contrary.

With regard to the rejection based on Stamatoyannopoulos in view of Greisman, Applicants reiterate that Stamatoyannopoulos teaches away from complexes of non-naturally occurring exogenous molecules with cellular chromatin as claimed. Greisman does not cure the defects of the primary reference. In particular, there is no discussion in Greisman about the target sites being sensitive to probes as claimed.

Applicants submit the Examiner has chosen bits and pieces of the cited references to arrive at the allegation that this combination of references suggests the claimed subject matter. This is improper. As stated in *KSR*, "a patent composed of several elements is not

proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." *KSR*, page 14. The Federal Circuit has consistently reversed a finding of obviousness, even when all claimed elements are individually present in the references. See, e.g., *In re Kotzab*, 55 USPQ2d 1313, 1317 (Fed. Cir. 2000). Thus, a rejection cannot be predicated on the mere identification of individual components of claimed limitations. Rather, particular findings must be made as to the reason the skilled artisan, with no knowledge of the claimed subject matter, would have selected these components for combination in the manner.

For at least the above reasons, withdrawal of the rejections under 35 U.S.C. §103(a) is respectfully requested.

CONCLUSION

For the reasons set forth herein, Applicants believe that the claims under consideration recite statutory subject matter, are novel and are non-obvious. Accordingly, allowance of the claims under consideration, and rejoinder and allowance of the withdrawn claims, are requested.

Respectfully submitted,

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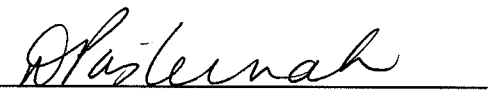
By: 

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